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<input type="checkbox"/>	L1	(curtiss\$ or gurtis\$).in.	1110
<input type="checkbox"/>	L2	L1 and salmonel\$	54
<input type="checkbox"/>	L3	L2 and system\$	35
<input type="checkbox"/>	L4	L2 and limit\$	28
<input type="checkbox"/>	L5	L4 and l3	27
<input type="checkbox"/>	L6	trans\$.clm. and (repressor or regulator or lethal or viability or death or killing or inhibiting or lethal\$).clm.	8154
<input type="checkbox"/>	L7	L6 and (heterologous or foreign or desired or antigen or product or expression or expressing or express).clm.	3551
<input type="checkbox"/>	L8	L7 and (prokaryote or procaryote or bacteria or gram or salmonella or shigella or bacterium or cell).clm.	3165
<input type="checkbox"/>	L9	trans\$.clm. same (repressor or regulator or lethal or viability or death or killing or inhibiting or lethal\$).clm.	2617
<input type="checkbox"/>	L10	L9 same (prokaryote or procaryote or bacteria or gram or salmonella or shigella or bacterium or cell).clm.	867
<input type="checkbox"/>	L11	L10 same (heterologous or foreign or desired or antigen or product or expression or expressing or express).clm.	419
<input type="checkbox"/>	L12	L11 and (environment\$ or induction or induced or limit\$ or premissive).clm.	88
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<input type="checkbox"/>	L14	L11 same (environment\$ or induction or induced or limit\$ or premissive).clm.	34
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END OF SEARCH HISTORY

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- ☐ 1. [20040208897](#). 15 Jul 03. 21 Oct 04. Recombinant bacterial system with environmentally limited viability. [Curtiss, Roy III](#), et al. 424/200.1; 435/252.33 435/488 A61K039/02 C12N015/74 C12N001/21.
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- ☐ 2. [20040137003](#). 12 Jan 04. 15 Jul 04. Regulated antigen delivery system (rads). [Curtiss III, Roy](#). 424/184.1; A61K048/00 A01N063/00 A61K039/00 A61K039/38.
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- ☐ 3. [20040120962](#). 15 Apr 03. 24 Jun 04. Modulation of immune responses to foreign antigens expressed by recombinant attenuated bacterial vectors. [Curtiss, Roy III](#), et al. 424/184.1; A61K039/00 A61K039/38.
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- ☐ 5. [20030031683](#). 03 May 02. 13 Feb 03. Recombinant vaccines comprising immunogenic attenuated bacteria having RpoS positive phenotype. [Curtiss, Roy III](#), et al. 424/200.1; 424/258.1 424/93.2 435/252.3 435/252.8 435/471 435/897 A61K048/00 A01N063/00 A61K039/02 C12N001/20 A61K039/112 C12N015/74 C12N001/00.
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- ☐ 9. [6610529](#). 06 Dec 96; 26 Aug 03. Recombinant bacterial system with environmentally limited viability. [Curtiss, III; Roy](#), et al. 435/252.3; 424/257.1 424/258.1 424/93.1 424/93.2 424/93.48 435/442 435/471 435/481 435/69.1. C12N001/21 A01N063/00 A61K039/108 C12P012/06.
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SALMONELS	0
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PGPUB-DOCUMENT-NUMBER: 20030082511
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030082511 A1

TITLE: Identification of modulatory molecules using inducible promoters

PUBLICATION-DATE: May 1, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Brown, Steven J.	San Diego	CA	US
Dunnington, Damien J.	San Diego	CA	US
Clark, Imran	San Diego	CA	US

APPL-NO: 09/965201 [PALM]
DATE FILED: September 25, 2001

INT-CL: [07] C12 Q 1/00, C12 Q 1/68

US-CL-PUBLISHED: 435/4; 435/6
US-CL-CURRENT: 435/4; 435/6

REPRESENTATIVE-FIGURES: NONE

ABSTRACT:

Methods for identifying an ion channel modulator, a target membrane receptor modulator molecule, and other modulatory molecules are disclosed, as well as cells and vectors for use in those methods. A polynucleotide encoding target is provided in a cell under control of an inducible promoter, and candidate modulatory molecules are contacted with the cell after induction of the promoter to ascertain whether a change in a measurable physiological parameter occurs as a result of the candidate modulatory molecule.

US-PAT-NO: 5672345

DOCUMENT-IDENTIFIER: US 5672345 A

TITLE: Selective maintenance of a recombinant gene in a population of vaccine cells

DATE-ISSUED: September 30, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
<u>Curtiss, III; Roy</u>	St. Louis	MO		

US-CL-CURRENT: 424/93.2; 435/252.3, 435/69.1, 435/71.2

CLAIMS:

I claim:

1. A live bacterial carrier for a vaccine for immunizing an individual, said carrier comprising an avirulent derivative of a pathogenic strain of bacteria characterized by:

a) a lack of a functioning native chromosomal gene encoding a first enzyme which is a .beta.-aspartic semialdehyde dehydrogenase (Asd);

b) the presence of a first recombinant gene encoding a second Asd enzyme wherein the first recombinant gene cannot recombine to replace the defective chromosomal gene;

c) the presence of a second recombinant gene encoding a desired polypeptide; and

d) physical linkage between the first recombinant gene and the second recombinant gene, wherein loss of the first recombinant gene causes the bacteria to lyse when in an environment which requires expression of said first recombinant gene for cell survival.

2. The live bacterial carrier according to claim 1 wherein said bacterial carrier is formulated in a pharmaceutically acceptable excipient in a pharmacologically effective dose.

3. The live bacterial carrier of claim 1, wherein the avirulent derivative of a pathogenic strain of bacteria is a Salmonella.

4. The live bacterial carrier of claim 3, wherein the first recombinant gene encodes Asd derived from Streptococcus mutans.

5. The live bacterial carrier of claim 4, wherein the second recombinant gene encodes an antigenic determinant encoded with the spaA gene of S. mutans.

6. The live bacterial carrier of claim 5, wherein the first recombinant gene encodes Asd derived from S. typhimurium.

7. A composition for stimulating an immune response in an individual

comprising a live avirulent derivative of a pathogenic strain of bacteria characterized by:

a) a lack of a functioning native chromosomal gene encoding a first enzyme which is a .beta.-aspartic semialdehyde dehydrogenase (Asd);

b) the presence of a first recombinant gene encoding a second Asd enzyme wherein the first recombinant gene cannot recombine to replace the defective chromosomal gene;

c) the presence of a second recombinant gene encoding a desired polypeptide; and physical linkage between the first recombinant gene and the second recombinant gene, wherein loss of the first recombinant gene causes the bacteria to lyse when in an environment which requires expression of said first recombinant gene for cell survival.

8. The composition of claim 7, wherein the avirulent derivative of a pathogenic strain of bacteria is a Salmonella.

9. The composition of claim 8, wherein the first recombinant gene encodes Asd derived from *S. mutans*.

10. The composition of claim 9, wherein the second recombinant gene encodes an antigenic determinant encoded within a *spaA* gene of *S. mutans*.

11. The composition of claim 10, wherein the first recombinant gene encodes Asd derived from *S. typhimurium*.

12. A method of immunizing an individual comprising administering the live bacterial carrier for a vaccine of claim 1 to the individual.

13. A method of stimulating the immune system of an individual comprising administering the composition of claim 7 to the individual.

14. A method of preparing a bacterial carrier for a vaccine for immunization of an individual, said method comprising:

a) providing an avirulent derivative of a pathogenic strain of bacteria characterized by:

1) a lack of a functioning native chromosomal gene encoding a first enzyme which is a .beta.-aspartic semialdehyde dehydrogenase (Asd)

2) the presence of a first recombinant gene encoding a second Asd enzyme wherein the first recombinant gene cannot recombine to replace the defective chromosomal gene;

3) the presence of a second recombinant gene encoding a desired polypeptide; and

4) physical linkage between the first recombinant gene and the second recombinant gene, wherein loss of the first recombinant gene causes the bacteria to lyse when in an environment which requires expression of said first recombinant gene for cell survival;

b) providing a suitable excipient; and

c) mixing the bacteria with the excipient in a suitable pharmacologic dose.

15. An immunogenic composition comprising an avirulent derivative of a pathogenic strain of bacteria characterized by:

a) a lack of a functioning native chromosomal gene encoding a first enzyme which is a .beta.-aspartic semialdehyde dehydrogenase (Asd);

b) the presence of a first recombinant gene encoding a second Asd enzyme wherein the first recombinant gene cannot recombine to replace the defective chromosomal gene;

c) the presence of a second recombinant gene encoding a desired polypeptide; and

d) physical linkage between the first recombinant gene and the second recombinant gene, wherein loss of the first recombinant gene causes the bacteria to lyse when in an environment which requires expression of said first recombinant gene for cell survival.

16. The composition of claim 15 wherein the second recombinant gene encodes an antigenic determinant encoded within a spaA gene of S. mutans.

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L2: Entry 19 of 54

File: USPT

Aug 12, 1997

US-PAT-NO: 5656488

DOCUMENT-IDENTIFIER: US 5656488 A

TITLE: Recombinant avirulent salmonella antifertility vaccines

DATE-ISSUED: August 12, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
<u>Curtiss, III; Roy</u>	St. Louis	MO		
Tung; Kenneth S. K.	Charlottesville	VA		

US-CL-CURRENT: 435/252.33; 424/184.1, 424/200.1, 435/252.3, 435/252.8, 435/69.3, 530/395

CLAIMS:

We claim:

1. An avirulent microbe derived from a pathogenic gram negative microorganism selected from the group consisting of Salmonella, Escherichia, and Salmonella-Escherichia hybrids comprising a recombinant expression system which encodes at least one gamete-specific antigen that is displayed on the surface of gametes exposed during the process leading to fertilization, wherein the avirulent microbe, upon administration to an individual, is capable of colonizing a lymphoreticular tissue and eliciting a mucosal immune response.
2. An avirulent microbe according to claim 1, wherein the avirulent microbe lacks a functioning native chromosomal gene encoding beta-aspartate semialdehyde dehydrogenase (Asd), and further wherein the microbe comprises a recombinant gene encoding a functional Asd polypeptide, the recombinant gene being linked to one or more genes encoding one or more gamete-specific antigens.
3. An avirulent microbe according to claim 1, wherein the avirulent microbe comprises a mutated cya gene such that the microbe is substantially incapable of producing functional adenylate cyclase.
4. An avirulent microbe according to claim 1, wherein the avirulent microbe comprises a mutated crp gene such that the microbe is substantially incapable of producing functional cyclic AMP receptor protein.
5. An avirulent microbe according to claim 2, wherein the avirulent microbe further comprises a mutated cya gene and a mutated crp gene such that the microbe is substantially incapable of producing functional adenylate cyclase and functional cyclic AMP receptor protein.
6. An avirulent microbe according to claim 1, wherein the microbe is *S. typhimurium*.

7. An avirulent microbe according to claim 1, wherein the microbe is an E. coli-Salmonella hybrid.
8. An avirulent microbe according to claim 1, wherein the gamete-specific antigen is lactic dehydrogenase-C.
9. An avirulent microbe according to claim 1, wherein the gamete-specific antigen is SP-10.
10. An avirulent microbe according to claim 1 wherein the gamete-specific antigen is ZP-3.
11. An avirulent microbe according to claim 5, wherein the gamete-specific antigen is lactic dehydrogenase-C.
12. An avirulent microbe according to claim 5, wherein the gamete-specific antigen is SP-10.
13. An avirulent microbe according to claim 5 wherein the gamete-specific antigen is ZP-3.
14. A vaccine composition comprising a therapeutically effective amount of an avirulent microbe according to claim 1, in combination with a pharmaceutically acceptable vehicle.
15. A vaccine composition comprising a therapeutically effective amount of an avirulent microbe according to claim 5, in combination with a pharmaceutically acceptable vehicle.
16. A method for inducing an antifertility state in a vertebrate subject, said method comprising administering to said subject an effective amount of a vaccine composition according to claim 14.
17. A method for inducing an antifertility state in a vertebrate subject, said method comprising administering to said subject, an effective amount of a vaccine composition according to claim 15.
18. A method according to claim 16, wherein the gamete-specific antigen is lactic dehydrogenase-C.
19. A method according to claim 16, wherein the gamete-specific antigen is SP-10.
20. A method according to claim 16, wherein the gamete-specific antigen is ZP-3.
21. A method according to claim 17, wherein the gamete-specific antigen is lactic dehydrogenase-C.
22. A method according to claim 17, wherein the gamete-specific antigen is SP-10.
23. A method according to claim 17, wherein the gamete-specific antigen is ZP-3.

24. An avirulent microbe according to claim 1 wherein the gamete-specific antigen is a sperm-specific antigen.

25. An avirulent microbe according to claim 24 wherein the sperm-specific antigen is selected from the group consisting of lactate dehydrogenase-C and SP-10.

26. An avirulent microbe according to claim 1 wherein the gamete-specific antigen is an ovum-specific antigen.

27. An avirulent microbe according to claim 5 wherein the gamete-specific antigen is a sperm-specific antigen.

28. An avirulent microbe according to claim 5 wherein the sperm-specific antigen is selected from the group consisting of lactate dehydrogenase-C and SP-10.

29. An avirulent microbe according to claim 5 wherein the gamete-specific antigen is an ovum-specific antigen.

30. A vaccine composition comprising a therapeutically effective amount of an avirulent microbe according to claim 24, in combination with a pharmaceutically acceptable vehicle.

31. A vaccine composition comprising a therapeutically effective amount of an avirulent microbe according to claim 25, in combination with a pharmaceutically acceptable vehicle.

32. A vaccine composition comprising a therapeutically effective amount of an avirulent microbe according to claim 26, in combination with a pharmaceutically acceptable vehicle.

33. A vaccine composition comprising a therapeutically effective amount of an avirulent microbe according to claim 27, in combination with a pharmaceutically acceptable vehicle.

34. A vaccine composition comprising a therapeutically effective amount of an avirulent microbe according to claim 28, in combination with a pharmaceutically acceptable vehicle.

35. A vaccine composition comprising a therapeutically effective amount of an avirulent microbe according to claim 29, in combination with a pharmaceutically acceptable vehicle.

36. A method according to claim 16, wherein the gamete-specific antigen is a sperm-specific antigen.

37. A method according to claim 36, wherein the sperm-specific antigen is selected from the group consisting of lactate dehydrogenase-C and SP-10.

38. A method according to claim 16 wherein the gamete-specific antigen is an ovum-specific antigen.

39. A method according to claim 17, wherein the gamete-specific antigen is a sperm-specific antigen.

40. A method according to claim 17, wherein the sperm-specific antigen is selected from the group consisting of lactate dehydrogenase-C and SP-10.
41. A method according to claim 17 wherein the gamete-specific antigen is an ovum-specific antigen.
42. The avirulent microbe according to claim 1 wherein said avirulent microbe is capable of eliciting a mucosal immune response to lactic dehydrogenase-C.
43. The avirulent microbe according to claim 1 wherein said avirulent microbe is capable of eliciting a mucosal immune response to SP-10.
44. The avirulent microbe according to claim 1 wherein said avirulent microbe is capable of eliciting a mucosal immune response to ZP-3.
45. A vaccine composition comprising a therapeutically effective amount of an avirulent microbe according to claim 42.
46. A vaccine composition comprising a therapeutically effective amount of an avirulent microbe according to claim 43.
47. A vaccine composition comprising a therapeutically effective amount of an avirulent microbe according to claim 44.
48. A method for inducing an antifertility state in a vertebrate subject, said method comprising administering to said subject an effective amount of a vaccine composition according to claim 45.
49. A method for inducing an antifertility state in a vertebrate subject, said method comprising administering to said subject an effective amount of a vaccine composition according to claim 46.
50. A method for inducing an antifertility state in a vertebrate subject, said method comprising administering to said subject an effective amount of a vaccine composition according to claim 42.

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**** See image for Certificate of Correction ****TITLE: Avirulent microbes and uses therefor: salmonella typhi

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INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
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CLAIMS:

We claim:

1. An immunogenic composition for the immunization of an individual comprising a live avirulent S. typhi obtained from a pathogenic S. typhi strain, said avirulent S. typhi made avirulent by of an inactivating mutation in the structural cya gene and an inactivating mutation in the structural crp gene.
2. An immunogenic composition according to claim 1, wherein said avirulent S. typhi is a recombinant gene from an agent pathogenic to said individual, to produce an antigen which induces an immune response in said individual against said pathogen.
3. A method for stimulating the immune system of an individual to respond to an immunogenic antigen of S. typhi comprising administering to said individual the immunogenic composition comprising a live avirulent S. typhi obtained from a pathogenic S. typhi strain, said avirulent S. typhi made avirulent by an inactivating mutation in the structural cya gene and an inactivating mutation in the structural crp gene.
4. A method for stimulating the immune system of an individual to respond to an immunogenic antigen of a pathogen comprising administering to said individual an immunogenic composition comprising a live avirulent S. typhi obtained from a pathogenic S. typhi strain, said avirulent S. typhi made avirulent by an inactivating mutation in the structural cya gene and an inactivating mutation in the structural crp gene wherein said avirulent S. typhi expresses a recombinant gene from an agent pathogenic to said individual, to produce an antigen which induces an immune response in said individual against said pathogen.
5. An isolated avirulent strain of S. typhi obtained from a pathogenic strain of S. typhi said avirulent S. typhi made avirulent by an inactivating mutation in the structural cya gene and an inactivating mutation in the structural crp gene.

6. The isolated avirulent strain of *S. typhi* of claim 5 which expresses a recombinant gene from an agent pathogenic to an individual, to produce an antigen which induces an immune response in said individual against said pathogen.
7. A strain according to claim 6 wherein the *S. typhi* contains a chromosomal mutation which is lethal and which is balanced by a vector borne gene which complements the lethal mutation to constitute a balanced-lethal host-vector system.
8. A strain according to claim 7 wherein cells of the strain;
 - (a) lack a functioning native chromosomal gene encoding .beta.-aspartate semialdehyde dehydrogenase (asd);
 - (b) have present an exogenously introduced gene encoding a functional Asd polypeptide which phenotypically complements the chromosomal asd mutation, but which cannot replace the defective chromosomal gene by recombination; and
 - (c) have a physical linkage between the genes encoding the functional Asd polypeptide and the immunogenic antigen, wherein the loss of the gene encoding the functional Asd polypeptide causes the cells to lyse when the cells are in an environment in which the lack of functional Asd causes the cells to lyse.
9. A strain according to claim 5 that has the characteristics of .chi.3927.
10. An immunogenic composition according to claim 1 comprised of a strain according to claim 9.
11. A method of preparing an immunogenic composition by suspending in a physiological excipient, an avirulent *S. typhi* obtained from a pathogenic strain of *S. typhi*, the avirulent *S. typhi* having an inactivating mutation in the structural cya gene and an inactivating mutation in the structural crp gene.
12. A method according to claim 4 wherein said live avirulent *S. typhi* also
 - (a) lacks a functioning native chromosomal gene encoding .beta.-aspartate semialdehyde dehydrogenase (asd);
 - (b) has present an exogenously introduced gene encoding a functional Asd polypeptide which phenotypically complements the chromosomal asd mutation, but which cannot replace the defective chromosomal gene by recombination; and
 - (c) has physical linkage between the genes encoding the functional Asd polypeptide and the immunogenic antigen, wherein the loss of the gene encoding the functional Asd polypeptide causes the cells to lyse when the cells are in an environment in which the lack of functional Asd causes the cells to lyse.